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## For Obesity-Related Cancers, Both BMI and Weight Gain Matter

— Still, effects differ among different tumor types

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May 29, 2018

A high body-mass index (BMI) as well as gaining large amounts of weight irrespective of starting BMI both contribute to obesity-related cancers, although not necessarily the same ones, a large epidemiological study from Norway suggested.

During an average follow-up of 18 years, an analysis of 137,708 women showed that participants with obesity had a more than two-fold risk of developing endometrial cancer compared with normal-weight women, at a hazard ratio (HR) of 2.18 (95% CI 1.59-2.98;  $P < 0.001$ ), reported Marisa da Silva, of Arctic University of Norway in Tromsø, and colleagues at the European Association for the Study of Obesity conference in Vienna.

Postmenopausal women with obesity were 20% more likely to develop breast cancer compared with normal-weight women, at an HR of 1.20 (95% CI 1.00-1.44), while women with obesity were also 95% more likely to develop kidney cancer over the study interval, at an HR of 1.95 (95% CI 1.26-3.02).

But the most novel finding from the analysis was a major increase in pancreatic cancer among women who gained 10 kg or more over a period of 6 years, the researchers reported. At an average follow-up of 13.7 years, the risk of pancreatic cancer was 91% higher in women who gained at least 10 kg over 6 years than it was for women who maintained a stable weight, at an HR of 1.91 (95% CI 1.11-3.30) -- even though there was no association between baseline BMI and increased risk of pancreatic cancer.

"Our finding of increased risk of pancreatic cancer by high weight gain is of special importance, as this has not been assessed in such detail in women before," da Silva and colleagues stated. "Maintaining stable weight in middle adulthood, irrespective of baseline BMI status, as well as avoiding excess body weight are both of importance for the prevention of several obesity-related cancers in women."

Data from the Norwegian Women and Cancer (NOWAC) study was analyzed to identify obesity-related cancers in a nationally representative, population-based cohort of women between ages 30 and 70.

The participants completed an enrollment questionnaire and were followed up with a second questionnaire 5 to 8 years later. The questionnaire included information on weight, height, reproductive history, use of medication, and lifestyle issues. Questionnaires were completed between 1991 and 2014, and both BMI and weight change over a 6-year interval were determined.

related cancers in a sample of 80,930 women over an average follow-up of 13.7 years. Compared with normal-weight women, obesity increased the overall risk of obesity-related cancers by 24%, at an HR of 1.24 (95% CI 1.14-1.34;  $P < 0.001$ ). In contrast, obesity was not significantly associated with either ovarian or colorectal cancer. The authors noted that both ovarian and rectal cancers have been defined as "obesity-related cancers," but were not associated with either excess body weight or weight gain in this particular sample of women.

Significant weight gain over a 6-year interval also increased the risk of women developing any obesity-related cancer by 14%, at an HR of 1.14 (95% CI 1.05-1.25) for those who gained between five and 10 kg and by 16%, at an HR of 1.16 (95% CI 1.04-1.31;  $P = 0.016$  for both endpoints) for those who gained 10 kg or more. Moderate weight gain of less than 10 kg also increased the risk of postmenopausal breast cancer by 20%, at an HR of 1.20 (95% CI 1.01-1.43), while a weight gain of 10 kg or more increased postmenopausal breast cancer risk by 36%, at an HR of 1.36 (95% CI 1.08-1.71;  $P = 0.041$  for both endpoints).

The same categories of weight gain also increased the risk of endometrial cancer to a similar extent: by 27% for moderate weight gain (HR 1.25; 95% CI 1.01-1.61) and by 40% for high weight gain (HR 1.40; 95% CI 1.04-1.88;  $P = 0.013$  for both endpoints). Interestingly, moderate -- although not high -- levels of weight gain increased the risk of colorectal cancer by 24% (HR 1.24; 95% CI 1.05-1.48). Moderate weight gain also increased the risk of pancreatic cancer by 60% (HR 1.60; 95% CI 1.03-2.47;  $P = 0.114$ ).

Da Silva speculated in an email to *MedPage Today* that the biological mechanisms through which weight gain might affect pancreatic cancer risk could be related to insulin levels and higher bioavailability of insulin-like growth factor, which play a more essential role in weight gain than in BMI per se.

Limitations of the study, she and her colleagues said, include the fact that it was not possible to differentiate between intentional and unintentional weight loss and that unintentional weight loss could be a preclinical symptom of cancer. "I believe it is important to have a long-term perspective when it comes to weight management, and regardless of BMI, having a stable weight -- not only being within a normal weight category -- is of importance for cancer prevention," da Silva noted.

"Of course, losing weight for someone with overweight or obesity has health benefits, but having a stable weight is a first step and of importance, especially since most women gain weight through middle adulthood."

Jennifer Ligibel, MD, of Dana-Farber Cancer Institute in Boston, who is chair of the American Society of Clinical Oncology's Obesity and Energy Balance Subcommittee, told *MedPage Today* that this study, like many of the studies from Scandinavian countries, is significant, because it has so many weight measurements and has "excellent and consistent follow-up, which is something that researchers in the U.S. have had a difficult time achieving.

"Because of the [Scandinavian] healthcare system, [these researchers] were able to look at weight at different points in life and weight change, so this paper has some nice information about some of the weight patterns that occur over time that are often not seen in other datasets just because we don't have these sequential measures on such a large proportion of the cohort," said Ligibel, who wasn't involved with the study.

However, she also said that physicians have to put this single study into context, since there are now "thousands of studies" that have contributed to the large meta-analyses looking at the links between body weight, weight gain, and cancer risk, which

Da Silva and Ligibel reported having no conflicts of interest.

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\_\_\_\_\_ LAST UPDATED 05.31.2018

**Primary Source**

*European Association for the Study of Obesity*

Source Reference: [Da Silva M, et al "BMI, weight change, and obesity-related cancer risk in the Norwegian Women and Cancer \(NOWAC\) study. European Association for the Study of Obesity. Abstract T2P14.](#)